

COUNTY OF LOS ANGELES - DEPARTMENT OF MENTAL HEALTH

OFFICE OF THE MEDICAL DIRECTOR

3.3 PARAMETERS FOR THE USE OF ANTIPSYCHOTIC MEDICATIONS

Revised January 5, 2011

I. GENERAL PARAMETERS FOR USE

- A. Definition:** Antipsychotic medications in this parameter include: phenothiazines, haloperidol, thiothixene, loxapine; and selected newer antipsychotic medications (aripiprazole, asenapine, clozapine, iloperidone, olanzepine, quetiapine, paliperidone, risperidone, and ziprasidone).
- B. Essential Use:** Antipsychotic medications should almost always be tried in individuals with a diagnosis of schizophrenia or schizoaffective disorder if positive or negative symptoms are present, or have been present in the last year, and no contraindications to their use exist.
- C. Optional Use:**
1. Antipsychotic medications may be continued in individuals with a diagnosis of schizophrenia or schizoaffective disorder who are asymptomatic for greater than one year if the risks of relapse to outweigh the risks and discomfort of medication use.
 2. Antipsychotic medications may be tried in individuals with diagnoses other than schizophrenia or schizoaffective disorder in which psychotic symptoms (including negative symptoms) are present.
 3. Antipsychotic medications may be used to treat mania in bipolar disorder, manic phase, or mixed type; and prophylactically to decrease the likelihood of developing mania during antidepressant treatment for bipolar disorder, depressed phase; and as prophylaxis against developing further mood episodes for bipolar disorder in partial or complete remission.
 4. Specific antipsychotic medications may be used to augment a suboptimal antidepressant response to antidepressant medications when changing the type or dose of the antidepressant is not clinically indicated.

II. MULTIPLE CONCURRENT ANTIPSYCHOTIC MEDICATIONS

1. Only one antipsychotic medication should be used at any one time, except during brief (= or <90 days) transition from one to another or in exceptional circumstances. The reason for concurrent dosing should be well documented in the clinical record.
2. Exceptional circumstances are those when successive trials of monotherapy with available newer antipsychotic medications at

appropriate dose and duration have been unsuccessful.

3. Prior to initiating concurrent treatment with 2 or more newer antipsychotic medications for individuals who have not responded to treatment with single newer antipsychotic medications, a trial of clozapine should be considered and initiated unless there are significant contraindications that have clearly been documented as such in the clinical record.
4. Whenever 2 or more antipsychotics are prescribed simultaneously, reasons for this polypharmacy and estimated duration should be periodically (at least every 90 days) and fully documented in the clinical record.

III. SELECTION OF ANTIPSYCHOTIC MEDICATIONS

1. Antipsychotic medications should be selected based upon effect profiles that appear best suited to a specific application, when other antipsychotic medications are contraindicated or unavailable, or when patients are already stabilized and doing well on a particular antipsychotic medication and are not at undue risk for untoward effects.
2. A different antipsychotic medication should be tried in individuals currently receiving an antipsychotic medication if symptoms persist and are clinically significant more than 6 months after an adequate trial of that antipsychotic medication, and there are no contraindications to switching.
3. An antipsychotic medication with a low incidence of extrapyramidal side effects should be substituted if clinically significant parkinsonism, dystonia, or akathisia is present and cannot be effectively managed by lowering the dose of the current antipsychotic medication, or by adding anti-parkinsonian agents.
4. Clozapine should be substituted in instances in which tardive dyskinesia is present, if no contraindications to clozapine are present.
6. In cases in which tardive dyskinesia is present and contraindications to use of clozapine are present, another antipsychotic medication with a low incidence of extrapyramidal side effects should be substituted.

ADDITIONAL PRECAUTIONS WITH THE USE OF ANTIPSYCHOTIC MEDICATIONS

C. Black Box Warning: Because of concerns that treatment of elderly patients with dementia-related psychosis treated with antipsychotic drugs may be at an increased risk of death, documentation of the reason for selection and

consideration of the risk of these medications in such an individual should be documented in the clinical record.

D. Contraindications: Significant risk of untoward general medical effects relative to efficacy for certain older antipsychotic medications (chlorpromazine, thioridazine) should preclude their use, except in unusual situations that are adequately documented in the clinical record at least every 90 days.

IV. USE OF CLOZAPINE

A. Essential Use:

1. Clozapine should be tried if symptoms persist and are clinically significant more than 6 months after adequate trials of at least two other newer antipsychotic medications, and there are no contraindications to such treatment.
2. Clozapine should be tried if there is tardive dyskinesia that does not stabilize or reverse with switch to other antipsychotic medications with a low incidence of extrapyramidal side effects.

B. Optional Use: Clozapine may be tried for individuals with psychotic disorders who have persistent suicidal ideation or behaviors that have not been significantly diminished while using other antipsychotic medications.

C. Special Considerations: **Clozapine use and clinical documentation must be compliant with FDA mandated standards for registration, linkages, monitoring, and reporting.**

V. USE OF DEPOT ANTIPSYCHOTIC MEDICATIONS

A. Essential Use:

1. Use of long acting injectable antipsychotic medications should be limited to individuals with current non-adherence to antipsychotic medication as reported by client or others, leading to treatment failure as evidenced by hospitalizations, incarceration, or clinical non-response.
2. Long acting injectable antipsychotic medications should not be used concurrently with oral antipsychotic medications except during time limited (less than 60 days) switchover from oral to injectable medication.
3. Specific long acting injectable antipsychotic medication should be used only within programs that have the capacity to provide the necessary clinical and logistical support required by those medications.
 - a. Depot risperidone: Support for refrigeration and tracking (see appendix)

- b. Olanzapine long-acting injection (LAI): Post injection delirium/sedation syndrome (see appendix)

VI. ANTIPSYCHOTIC DOSAGES

1. The lowest effective dose of antipsychotic medication should be used in order to promote comfort and safety and to minimize the risks of EPS, tardive dyskinesia, and other untoward effects.
2. An adequate trial with a daily dose within the usual range for a specific antipsychotic medication should be attempted before using higher doses. Use of higher doses should be associated with appropriately increased monitoring of target symptoms and untoward effects and should not be continued for longer than 90 days in the absence of clinical improvement.
3. **Clozapine: Note: Please see attached 9/20/05 DMH Prescribing Guidelines For the Use of Clozapine**
An adequate trial with a daily dose (after titration) between 150 and 600 mg should be attempted before using higher doses. Doses above 900 mg daily have not been shown to be clearly more effective and therefore should be used only after obtaining a clozapine plasma level that establishes compliance, and documentation of rationale and estimated duration of trial.
4. **Olanzapine:** An adequate trial with a daily dose between 10 and 20 mg should be attempted before using higher doses. Doses above 40 mg daily have not been shown to be clearly more effective and therefore should not be used without documentation of rationale and estimated duration of trial. Olanzapine should not be used to treat dementia-related psychosis in older adults due to a higher reported incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, in this population.
5. **Quetiapine:** An adequate trial with a daily dose between 150 and 800 mg should be attempted before using higher doses. Doses above 900 mg daily have not been shown to be clearly more effective and therefore should not be used without documentation of rationale and estimated duration of trial. Quetiapine should not be used solely for the purpose of sedation, in the absence of other indications.
6. **Risperidone:** An adequate trial with a daily dose between 2 and 6 mg should be attempted before using higher doses. Doses above 12 mg daily have not been shown to be clearly more effective and therefore should not be used without documentation of rationale and estimated duration of trial.
7. **Ziprasidone:** An adequate trial with a daily dose of 40 mg bid should be attempted before using higher doses. Doses above 80 mg bid have not been shown to be clearly more effective and therefore

require clinical documentation of reasoning. Safety above 100 mg bid has not been established and such use therefore requires additional justification.

8. **Aripiprazole:** An adequate trial with a daily dose between 10 and 20 mg should be attempted before using higher doses. Doses above 30 mg daily have not been shown to be clearly more effective and therefore should not be used without documentation of rationale and estimated duration of trial.
9. **Asenapine:** An adequate trial of 5mg sublingually bid for schizophrenia and 10 mg sublingually for bipolar disorders should be attempted before using higher dosages.
10. **Iloperidone:** Iloperidone should be used only when antipsychotic medications with a side effect profile with lower incidence of prolongation of the QTc are contraindicated or not effective.

VII. GENERAL HEALTH-RELATED ASSESSMENT AND MONITORING FOR INDIVIDUALS RECEIVING ANTIPSYCHOTIC MEDICATIONS

1. Antipsychotic medication should be initiated and maintained only in circumstances that permit adequate general health-related assessment and monitoring that is consistent with DMH Parameters, [3.7 Parameters for General Health-Related Monitoring and Interventions in Adults.](#)

VIII. NONCOMPLIANCE WITH ANTIPSYCHOTIC MEDICATIONS

1. Assessment and interventions for non-compliance with antipsychotic medication involve clinical, social, and ethical considerations, and should involve close collaboration between the clinician, the individual being prescribed antipsychotic medication, and family and other involved individuals.
2. In situations in which individuals are noncompliant with assessment and monitoring recommendations, continued treatment with antipsychotic medications should be consistent with DMH Parameters for Non-Compliance: Medication Noncompliance.

Attachments:

1. [DMH Prescribing Guidelines for the Use of Clozapine 9/20/05](#)
2. Guidelines For The Authorization Of Treatment With Depot Risperdal Consta

References:

- [.03.3 Ref A ivaxi insert.pdf](#)
[.03.3 Ref B FAZACLO PI.pdf](#)
[.03.3 Ref C novardis.pdf](#)

**LOS ANGELES COUNTY
DEPARTMENT OF MENTAL HEALTH**

**Attachment 1 PRESCRIBING GUIDELINES FOR THE USE OF CLOZAPINE
9/20/05**

Section 1 – Community Agency Requirements

In order for Clozapine to be utilized in a Los Angeles County Department of Mental Health (LACDMH) program and/or contracted community agencies, the facility should:

- A. Maintain written policies and procedures for a Clozapine treatment program which describes linkage with a pharmacy and medical facility which will accept patients in an emergency. All procedures and agreements pertaining to this linkage must be clear.
- B. Establish a committee to review patients referred for a trial of Clozapine. This committee:
 - a. Is responsible for approving or disapproving requests for Clozapine trials within the agency.
 - b. Must make its decisions based on specified, enumerated criteria.
 - c. Must record each decision and the rationale for the decision.
- C. Register with Novartis Pharmaceuticals as part of their required "Clozapine Treatment System."
- D. Obtain an agreement to receive pharmaceutical services from a pharmacy registered with Sandoz Pharmaceuticals as part of their "Clozapine Treatment System."
- E. Obtain required consents.
 - a. It is necessary to obtain an informed consent before beginning treatment with Clozapine. Patients who are to receive Clozapine should be notified of the following in a clearly documented manner:
 - 1. The significant risk of developing agranulocytosis.
 - 2. Weekly blood tests are required to monitor for the occurrence of agranulocytosis at the onset of treatment. Later, adjustments of frequency may be considered. See: monitoring of hematological effects.
 - 3. Clozapine will be made available only through a special program designed to ensure the required blood monitoring.
 - 4. They are to immediately report the appearance of lethargy, weakness, fever, sore throat, malaise, mucous membrane ulceration, or other possible signs of infection.
 - 5. There is a significant risk of seizure during Clozapine treatment.

6. They are to avoid driving, and any other potentially hazardous activity, while beginning Clozapine until its effect on the sensorium is known.
7. There is a risk of orthostatic hypotension, especially during the period initial dose titration.
8. If they stop taking Clozapine for more than two (2) days, they should not start their medication at the same dosage, but should contact their physician for further instructions.
9. They should notify their physician if they are taking, or plan to take, any prescription or over-the-counter medications, drugs, or alcohol.
10. They should notify their physician if they become pregnant, or intend to become pregnant, during their therapy.
11. They should not breast feed an infant if they are taking Clozapine.

b. Release of information

Because data must be furnished to the National Clozapine Registry operated by Sandoz Pharmaceuticals, each patient must sign a DMH Consent for Release of Information which will allow the forwarding of this data.

Section II – Prescribing Standards

Agencies utilizing Clozapine must follow the complete manufacturer's recommendations on Clozapine in the current package insert. Prescribing standards are summarized in the following section. Some of the standards are adapted from the pharmaceutical company's recommendations. Additional LACDMH recommendations are indicated by an asterisk (*).

A. Indications for Clozapine treatment

a. Treatment refractory schizophrenia

1. The patient meets the DSM-IV criteria for the diagnosis of Schizophrenia or schizoaffective disorder.
2. The patient has had at least two drug treatment trials, each with a different standard antipsychotic drug product, carried out at an adequate dose for an adequate duration.
3. Clozapine may be chosen if the patient is unable to achieve recommended antipsychotic dosages on other medication due to intolerable effects.

b. Treatment of tardive dyskinesia

B. Contraindications

The patient has:

- a. History of a drug-induced blood dyscrasia*
- b. Severe debilitation*
- c. Uncontrolled seizure disorder

- d. White blood cell count of less than 3500 per mm
- e. History of a myeloproliferative disorder

C. Reinstitution of Clozapine

Clozapine therapy may not be reinstituted in any patient who has had a drop in white cell count below 3000 cells or granulocyte count below 1500 cells.

D. Pre-clozapine work-up*

The recommended pre-clozapine work-up should include:

- a. Physical examination within the past 30 days.
- b. Blood pressure supine and standing
- c. Oral temperature
- d. Pulse
- e. Electrocardiogram within the past six months
- f. Hematology battery including a complete blood count with differential and a comprehensive chemical panel including liver, kidney, and thyroid function tests
- g. Pregnancy test and, if indicated, appropriate contraceptives should be prescribed
- h. Check history of HIV testing

E. Dispensing and administering Clozapine

All procedures required by the manufacturer for physicians and pharmacists are to be followed, including the recommended dosages and titration schedules. Attending physicians must document their supervision of any residents involved in the dispensing or administering of Clozapine.

F. Monitoring

a. Hematologic effects

Complete blood counts with differential are drawn weekly for the first six months and then every two weeks if the patient has had acceptable WBC counts (i.e. the patient has never had a WBC count at or below 3000 or an absolute neutrophil count (ANC) at or below 1500) or a lapse in treatment greater than a month. If the patient has had an abnormal WBC or ANC count or has had a break in treatment of greater than one month, then the 6 month clock must be reset (see table 1 and figure 1). If during the bi-weekly period an abnormal blood event or a break in treatment greater than a year occurs, then weekly blood tests for 6 months must be reinstituted. After 6 months of continuous therapy, if acceptable WBC counts and ANC's (WBC count ≥ 3500 and ANC $\geq 2000/\text{mm}^3$) have been maintained during that period WBC count and ANC can be monitored every 4 weeks.

When treatment with Clozaril is discontinued (regardless of the reason), WBC count and ANC must be monitored weekly for at least 4 weeks from the day of discontinuation or until WBC count $\geq 3500/\text{mm}^3$ and ANC $\geq 2000/\text{mm}^3$.

The prescriber will initiate the following procedures when abnormalities are detected:

1. A drop of 3000 or more cells in the WBC count
or
The presence of immature white blood cell forms, regardless of WBC count
or
Three or more consecutive drops in the WBC count, or the size of the reduction
or
A drop in the WBC to below 3500 cells then:
 - (1) Repeat hematology tests
 - (2) Institute twice weekly monitoring
 - (3) Observe patient closely for signs of infection
2. A drop in WBC to below 3000 cells (neutropenia)
or
A drop in ANC to below 1500 cells (agranulocytosis) then:
 - (1) Stop Clozapine
 - (2) Repeat stat hematology tests
 - (3) Institute daily monitoring
 - (4) Observe patient closely
 - (5) Notify Clozapine Registry
3. A drop in the WBC to below 2000 cells
or
A drop in the ANC to below 1000 cells, then:
 - (1) Stop Clozapine 0 the patient cannot be retried on Clozapine
 - (2) Repeat hematology tests
 - (3) Institute daily hematology tests
 - (4) Hospitalize the patient in a facility which has 24 hr laboratory services and the ability to institute parenteral antibiotic therapy
 - (5) Monitor patient closely
 - (6) Notify the Clozapine Registry

b. Other effects*

1. Patient's vital signs should be closely monitored during initial titration periods and with dosage changes.
2. Comprehensive chemical panels including liver, kidney, and thyroid tests should be repeated after six months, twelve months, and then annually.

c. Concurrent medications

1. In many cases, there will be a transition period during which Clozapine is increased and another antipsychotic is decreased. *

2. Antidepressants should be prescribed only as a result of clear evidence of a major depression. *

3. Immuno-suppressants should not be used with Clozapine.

d. Criteria for Clozapine continuation *

1. Medi-Cal guidelines require significant improvement if patients are continued on Clozapine past 24 weeks. (Clinicians may use the BPRS to document their improvement.) Maintenance of Medi-Cal funding is important to our patients.

2. If severe tardive dyskinesia is the reason for initiating Clozapine treatment, substantial reduction in AIMS Global Score, with no deterioration in clinical condition, should be recorded to document the rationale of the treatment risk.

3. In the event that a partial response occurs, or that the patient has not responded by 24 weeks, or that dose titration has been difficult, consultation should be requested before continuation.

G. Consultants*

The Medical Director for LACDMH has established a Clozapine Consultant staff experienced clinically and administratively in the administration of Clozapine. For consultation and training call (213) 738-4603.

H. Facility approval for Clozapine use*

a. Directly-operated clinics

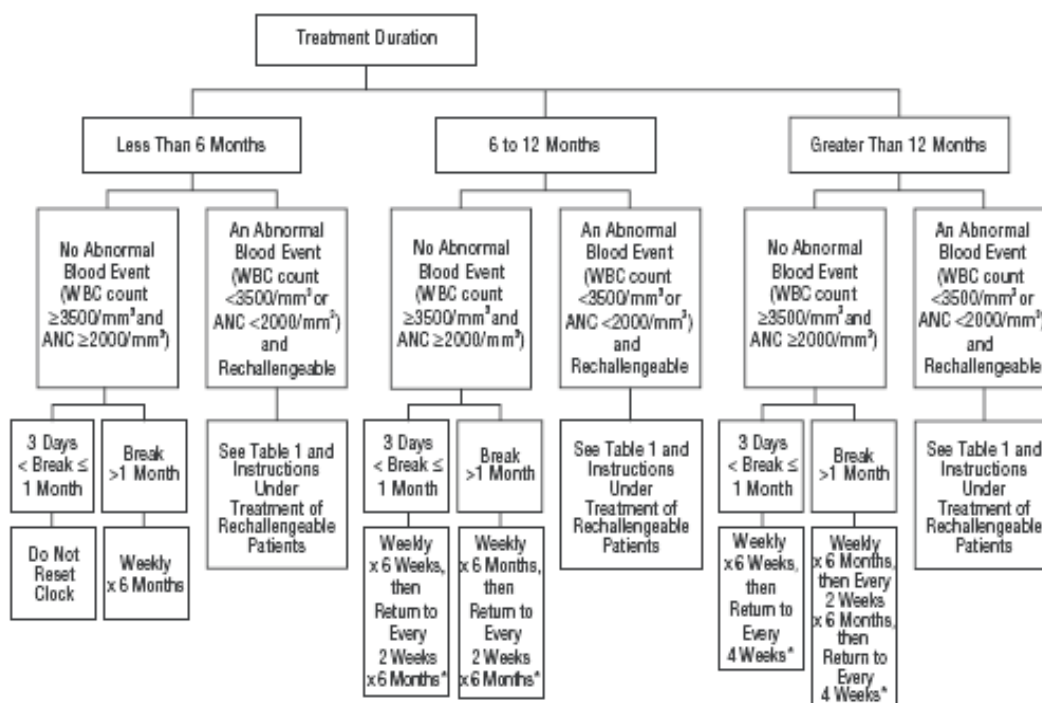
Prior to providing Clozapine, each directly-operated facility must obtain approval of their individual protocol from the Office of the Medical Director (OMD). The approval is based upon the facility's ability to meet the requirements outlined in the document.

b. Contract agency clinics

Facilities operated by agencies under contract to the LACDMH should also meet the requirements outlined in this document before prescribing Clozapine. Monitoring of adherence to these requirements and liability is the responsibility of the contract agency. On request, LACDMH staff are available for consultation to contract agencies to assist in meeting the requirements.

Table 1. Frequency of Monitoring Based on Stage of Therapy or Results from WBC Count and ANC Monitoring Tests		
Situation	Hematological Values for Monitoring	Frequency of WBC Count and ANC Monitoring
Initiation of therapy	WBC count $\geq 3500/\text{mm}^3$ and ANC $\geq 2000/\text{mm}^3$ Note : Do not initiate in patients with (1) history of myeloproliferative disorder or (2) clozapine-induced agranulocytosis or granulocytopenia.	Weekly for 6 months
6-12 months of therapy	All results for WBC count $\geq 3500/\text{mm}^3$ and ANC $\geq 2000/\text{mm}^3$	Every 2 weeks for 6 months
12 months of therapy	All results for WBC count $\geq 3500/\text{mm}^3$ and ANC $\geq 2000/\text{mm}^3$	Every 4 weeks ad infinitum
Immature forms present	N/A	Repeat WBC count and ANC
Discontinuation of Therapy	N/A	Weekly for at least 4 weeks from day of discontinuation or until WBC count $\geq 3500/\text{mm}^3$ and ANC $\geq 2000/\text{mm}^3$
Substantial drop in WBC count or ANC	Single drop or cumulative drop within 3 weeks of WBC count $\geq 3000/\text{mm}^3$ or ANC $\geq 1500/\text{mm}^3$	1. Repeat WBC count and ANC 2. If repeat values are $3000/\text{mm}^3 \leq \text{WBC count} < 3500/\text{mm}^3$ and $\text{ANC} > 2000/\text{mm}^3$, then monitor twice weekly
Mild leukopenia and/or Mild granulocytopenia	$3500/\text{mm}^3 > \text{WBC count} \geq 3000/\text{mm}^3$ and/or $2000/\text{mm}^3 > \text{ANC} \geq 1500/\text{mm}^3$	Twice weekly until WBC count $> 3500/\text{mm}^3$ and ANC $> 2000/\text{mm}^3$ then return to previous monitoring frequency
Moderate leukopenia and/or Moderate granulocytopenia	$3000/\text{mm}^3 > \text{WBC count} \geq 2000/\text{mm}^3$ and/or $1500/\text{mm}^3 > \text{ANC} \geq 1000/\text{mm}^3$	1. Interrupt therapy 2. Daily until WBC count $> 3000/\text{mm}^3$ and ANC $> 1500/\text{mm}^3$ 3. Twice weekly until WBC count $> 3500/\text{mm}^3$ and ANC $> 2000/\text{mm}^3$ 4. May rechallenge when WBC count $> 3500/\text{mm}^3$ and ANC $> 2000/\text{mm}^3$ 5. If rechallenged, monitor weekly for 1 year before returning to the usual monitoring schedule of every 2 weeks for 6 months and then every 4 weeks ad infinitum
Severe leukopenia and/or Severe granulocytopenia	WBC count $< 2000/\text{mm}^3$ and/or ANC $< 1000/\text{mm}^3$	1. Discontinue treatment and do not rechallenge patient 2. Monitor until normal and for at least four weeks from day of discontinuation as follows: • Daily until WBC count $> 3000/\text{mm}^3$ and ANC $> 1500/\text{mm}^3$ • Twice weekly until WBC count $> 3500/\text{mm}^3$ and ANC $> 2000/\text{mm}^3$ • Weekly after WBC count $> 3500/\text{mm}^3$
Agranulocytosis	ANC $< 500/\text{mm}^3$	1. Discontinue treatment and do not rechallenge patient 2. Monitor until normal and for at least four weeks from day of discontinuation as follows: • Daily until WBC count $> 3000/\text{mm}^3$ and ANC $> 1500/\text{mm}^3$ • Twice weekly until WBC count $> 3500/\text{mm}^3$ and ANC $> 2000/\text{mm}^3$ • Weekly after WBC count $> 3500/\text{mm}^3$

Figure 1. Resuming Monitoring Frequency After Interruption of Therapy



*Transitions to reduce frequency of monitoring only permitted if all WBC counts $\geq 3500/\text{mm}^3$ and ANC $\geq 2000/\text{mm}^3$.

COUNTY OF LOS ANGELES – DEPARTMENT OF MENTAL HEALTH
OFFICE OF THE MEDICAL DIRECTOR
PHARMACY SERVICES

November 21, 2010

TO: DMH Directly Operated and Contracted Clinics

FROM: Wayland Chan, Pharm.D.
Director of Pharmacy Services

SUBJECT: **GUIDELINES FOR THE AUTHORIZATION OF TREATMENT WITH DEPOT RISPERDAL CONSTA**

When prescribing Risperdal Consta (Consta), please use the following guidelines:

1. Program site must have compliant refrigeration capacity. Refrigerator must be in a secured locked area (e.g. medication room) and used only for medication (see *DMH Policy # 103.2*). Note: temperature must be monitored. Risperdal Consta is stable outside of refrigeration for a period of 7 days. Unused dosages may be used for other clients as long as the client is approved for using Consta.
2. Program site must have arrangements for delivery of Consta by a Pharmacy compliant with refrigeration requirements. Consta must be delivered under cold storage, with an ice chest.
3. If client is uninsured, they must be enrolled in the Janssen Patient Assistant Program.

If client is insured, program must confirm that health plan will cover the cost of medication.

Client must be prescribed oral risperidone **ONLY** (no other antipsychotic in addition to Consta) during the period of initiation. Also, once client is stable on Consta, (3 weeks) no additional antipsychotic is to be given, with the exception of short term oral risperidone when Consta dosage is to be increased.

4. Reasons for use; either of the following:
 - a. Current non-adherence to newer antipsychotic medication as reported by client or other, leading to treatment failure as evidenced by hospitalizations, incarceration, or clinical non-response.
 - b. For a client stabilized on decanoate antipsychotic medication (haloperidol or fluphenazine), risk of tardive dyskinesia outweighs risks of destabilization by medication switch, and where there is ongoing evidence of likely non-adherence with oral medication and/or treatment recommendations.

WC:hrs

c: Roderick Shaner, M.D.